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Comparison of the neuropathic pain symptoms and psychosocial impact of Trigeminal Neuralgia and Painful Post-Traumatic Trigeminal Neuropathy

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Abstract

Aims: To compare the impact of trigeminal neuralgia (TN) and painful post-traumatic trigeminal neuropathy (PPTTN) on psychological function and health-related quality of life (HRQoL) using a comprehensive quantitative assessment. **Methods:** This was a comparative cross-sectional study. Ninety-seven patients diagnosed with PPTTN and 40 patients with TN who sought treatment at an Orofacial Pain Clinic completed standardised self-report measures of pain intensity, neuropathic symptoms, pain self-efficacy, mood, and generic and oral HRQoL indicators. Differences between PPTTN and TN groups were tested, and associations between pain severity, psychological function and HRQoL examined. **Results:** The majority of PPTTN (66%) and TN patients (80%) were affected by orofacial pain. Pain attacks were more frequent in TN (71%) than PPTTN (28%) patients while numbness more common in PPTTN (51%) than TN (12%). Pain intensity was higher in TN for intermittent and affective pain dimensions. Both PPTTN and TN had a significant but comparable impact on patients' oral HRQoL. The burden of condition on overall health was significantly more pronounced in patients with TN than PPTTN, with differences evident in mobility and self-care domains. There was a trend showing that more TN (54%) than PPTTN (36%) patients reported signs of depression, but clinically significant anxiety was comparably high in both groups (34-39%). Anxiety and pain-self efficacy were closely related to oral and general health status in both groups. **Conclusions:** Both TN and PPTTN are associated with significant psychosocial burden and reduced HRQoL, indicating a need to develop effective treatments for neuropathic orofacial pain that target functional restoration.

Keywords: trigeminal neuralgia; post-traumatic trigeminal neuropathy; orofacial pain; trigeminal nerve injuries; psychosocial

Introduction

Chronic orofacial pain is multidimensional in nature, commonly involving a neuropathic pain (NP) component. The International Association for the Study of Pain (IASP) defines NP as “pain arising as a direct consequence of a lesion or disease affecting the somatosensory system”¹ Neuropathic pain of the orofacial region may be episodic, such as trigeminal neuralgias (TN), or continuous, which includes painful post-traumatic trigeminal neuropathy (PPTTN). Long-standing neuropathic orofacial pain may lead to significant changes in the individual’s psychological status, level of daily functioning and social interaction.² Accordingly, the relationships between NP conditions, such as TN and PPTTN, and psychological morbidities have increasingly become of interest to researchers.³

Trigeminal neuralgia (TN), although rare, is one of the well-known causes of severe orofacial pain. TN is defined by the International Association for the Study of Pain (IASP) as “a sudden, usually unilateral, severe, brief, stabbing recurrent pain in the distribution of one or more branches of the fifth cranial nerve”.⁴ Data from GP practices based in the United Kingdom drew an incidence of 8 per 10,000 people per year.⁵

According to The International Classification of Headache Disorders (ICHD)⁶, two types of classical trigeminal neuralgia are identified. The first type is purely paroxysmal without persistent background facial pain (classical trigeminal neuralgia, purely paroxysmal). It is usually responsive, at least initially, to pharmacotherapy (especially carbamazepine or oxcarbazepine). The second type (classical trigeminal neuralgia with concomitant continuous pain) is characterized by persistent background facial pain of moderate intensity in the affected area, which is less likely to be triggered by innocuous stimuli.⁶ Central sensitization may account

for the persistent facial pain. Additionally, symptomatic TN may occur secondary to the presence of an intracranial lesion compressing the trigeminal nerve at its root entry zone or secondary to multiple sclerosis.^{7, 8}

The neuropathic pain in TN patients is often excruciating, leading to severe distress which often causes anxiety, depression, and reduced quality of life.⁹⁻¹² It may lead to even suicide in some cases.¹³ TN patients usually seek health care from many providers with different specialties until proper diagnosis and management can be achieved. Dentists and physicians tend to first consider more common conditions likely to occur in the facial region (like toothache and temporomandibular disorders) rather than TN which is a relatively rare condition.¹⁴ Initial misdiagnosis may lead to unnecessary interventions in many patients, especially unneeded dental restorative and surgical procedures, which may add further to their suffering.¹⁵

Another prominent cause of orofacial NP is iatrogenic trigeminal nerve injuries (TNI), which may occur in relation to dental or oral surgical procedures, and often lead to painful post-traumatic trigeminal neuropathy (PPTTN). This damage may happen during implant placement, root canal treatment, orthognathic surgery, local anaesthetic injections and surgical removal of mandibular third molars.¹⁶ The incidence of painful neuropathy following TNIs is around 3-5%,¹⁷ and a key feature of PPTTN is the presence of continuous burning and/or shooting pain in an area of the trigeminal nerve distribution with a clear history of trauma. Clinically, there may be positive and/or negative changes in the neurological profile, which are the marking characteristic of PPTTN.¹⁸

Renton and Yilmaz¹⁹ have demonstrated the functional disability that patients with trigeminal nerve injuries may suffer from. This can include problems with speaking, eating,

drinking, make up application, and shaving, all of which lead to dramatic effects on personal and social lives. Smith and colleagues'³ study of patients with TNI indicated the increased risk of psychological dysfunction in patients with PPTTN as well as poor oral health-specific and overall quality of life.

As chronic orofacial pain extends over time, the psychosocial consequences of pain may become themselves etiological factors in the maintenance and enhancement of associated symptoms. Psychosocial factors are now believed to play an important role in the maintenance and amplification of the pain experience, and can affect the coping capabilities of the patient and the impairment of daily life activities.^{20, 21} Consequently, it is recognized that psychological factors associated with chronic orofacial pain need to be urgently addressed during diagnosis and treatment planning to achieve proper pain management.²²

Distinguishing between TN and trigeminal neuropathy arising from (dental) trauma is important from both a diagnostic and management perspective.¹⁸ Different orofacial pain conditions are often associated with varying degrees of psychological distress and (impaired) quality of life, as well as differences in disease perception and ways of coping with the painful disorder.⁹ Previous studies focussing on the psychosocial burden of patients with different types of orofacial pain have tended to compare neuropathic and non-neuropathic conditions,⁹ and where both TNI and TN patients have been considered they tend to be grouped together² or the samples were very small.²³ Comparisons of TN with other neuropathic disorders are rare. One recent study reported more severe pain intensity in TN than patients with burning mouth syndrome (BMS), although the psychosocial impact of these conditions was comparable.²⁴ The aim of this study was to evaluate the psychosocial impact of TN and TNI using a comprehensive

quantitative assessment, and to explore the relationship between neuropathic pain symptomatology, psychological function, and quality of life in TN and PPTTN patients.

Materials and Methods

Design

This was a comparative cross-sectional study, which evaluated the symptomatology and psychosocial impact of TN and PPTTN in patients who consecutively attended an orofacial Pain Clinic in South London (Dental Institute, King's College Hospital, London) during the period from January 2016 to August 2017. Data collection was done at the point of referral to the specialist centre. Written informed consent was obtained from all patients providing permission for their anonymised data to be used for research purposes. Ethical approval for the study was provided by the London–Dulwich Research Ethics Committee (REC reference 15/LO/1108).

Participants

Overall, 200 patients with a diagnosis of TN or PPTTN attended the service during the study periods under consideration for each (January 2016–August 2017 for TN patients, January 2016–February 2017 for PPTTN patients). This included 141 patients with PPTTN, 58 with TN, and one patient with both PPTTN and TN diagnoses. The latter was excluded from comparative analyses. Two patients with TN secondary to other causes with known psychiatric morbidity, specifically, patients who had multiple sclerosis (MS) before the onset of their TN, were excluded also, while one patient with PPTTN linked to bruxism was excluded. Bruxism is a parafunctional habit which is likely to induce painful TMJ dysfunction, but is not identified as a possible etiology for PPTTN. So, to avoid any symptom overlap which could affect the final results, we decided to exclude this case. All patients were examined thoroughly by specialized

pain consultants and referred to a neurologist for validation of the diagnosis where appropriate. Magnetic resonance imaging was used when indicated for exclusion of underlying causative lesions and detection of potential neurovascular compression of the trigeminal nerve. Patients were diagnosed according to the criteria of The International Classification of Headache Disorders, 3rd edition (beta version).⁶ The assessment protocol of trigeminal neuropathy used in the clinic has been published previously.²⁵ No patient was included in the study if they were affected by other potentially confounding facial pain conditions (other than headache or migraine) or severe mental illness. Demographic and clinical information were extracted from patients' records, including data concerning trigeminal nerve divisions involved in orofacial NP condition, side of the face affected, sensory deficits identified in clinical assessment (PPTTN), presence of migraines/headaches, and whether patients had other (bodily) chronic pain or any comorbid medical conditions.

Measures and Instruments

Participants of both groups were asked to complete a number of self-report, standardized questionnaires commonly used to measure pain experience, (oral) health-related quality of life (HRQoL) and psychological function in patients with chronic pain.³ Questionnaires were administered at patients' first clinic appointment either manually using hard copies or electronically using IMPARTS (an initiative funded by King's Health Partners to 'integrate mental and physical healthcare in research, training and clinical services').

Affective and Health Function Questionnaires

Depression was assessed using the 9-item Patient Health Questionnaire (PHQ-9),²⁶ a measure that assesses core diagnostic areas underlying clinical depression on a 9-item scale. Each item is

rated on a 4-point frequency scale ranging from 0 ('not at all') to 3 ('nearly every day'), with an overall score ranging from 0 to 27. Mild, moderate, moderately severe depression, and severe depression are indicated by scores of 5, 10, 15, and 20, respectively. The PHQ-9 has been validated in patients with a broad range of physical health problems, including chronic pain.²⁷

Anxious mood and behaviour was assessed with the 7-item Generalized Anxiety Disorder (GAD-7).²⁸ Response options for each item range from 0 ('not at all') to 3 ('nearly every day'), with a total score range of 0 to 21. Higher scores indicate more severe anxiety (disorder); a score of 8 or more indicates clinically significant levels of anxiety.²⁸ The GAD-7 has been recommended for the assessment of anxiety in patients with orofacial pain.²⁹

Oral health-related quality of life (OHRQoL) was assessed with the Oral Health Impact Profile (OHIP-14), a widely used questionnaire assessing the oral health domains of functional limitation, physical pain, psychological discomfort, physical disability, psychological disability, social disability and handicap.³⁰ The measure consists of 14 items, each scored on an ordinal frequency scale as follows: 0 = 'never'; 1 = 'hardly ever'; 2 = 'occasionally'; 3 = 'fairly often'; 4 = 'very often'. Summary variables computed for the OHIP-14 were an overall severity score of oral HRQoL impairment, calculated as the sum of all ordinal responses (range = 0 to 56), and an extent score determined by the number of items with 'fairly often' or 'very often' responses. The psychometric properties of the OHIP-14 are generally good.^{22, 31}

HRQOL was measured using the EQ-5D-5L, a generic health status questionnaire that consists of five dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Using a 5-point ordinal scale ('no problems', 'slight problems', 'moderate problems', 'severe problems' and extreme problems; coded from 0 to 4), respondents were asked

to select the level which best matched their health for each domain. For each patient, an overall health state valuation (EQ-Health), ranging from -0.285 for extreme problems in all domains to 1.000 for no problems in any domain, was calculated according to a value set recently developed for England populations.³² Patients also indicated their self-rated health on a 20-cm vertical visual analog scale (EQ-VAS) with worst (0) and best health (100) they could imagine as scale anchors.³³ The EQ-5D-5L has shown sufficient convergent validity to be used with patients with persistent orofacial pain.³⁴

Pain and Pain-Related Function Questionnaires

Patients who reported experiencing orofacial pain at the time of consultation were asked to complete measures gauging pain experience and pain-related function.

The sensory, affective, and evaluative qualities of pain were measured using the Short-Form McGill Pain Questionnaire – 2 (SF-MPQ-2), a 22-item revised version of the SF-MPQ that uses a 11-point numeric rating scale (NRS) on all items and includes symptoms relevant to neuropathic pain (Dworkin et al., 2009). An overall score is determined by the mean of all 22 items, with higher scores indicative of more severe symptoms. Four subscales have been established based on pain descriptors: continuous, intermittent, neuropathic, and affective. Subscales are scored by calculating the mean of the relevant items. There is support for the construct validity, convergent validity and reliability of the SF-MPQ-2 across many chronic pain conditions.^{35, 36}

Patients' current pain level and their average and strongest pain over the last month was measured using the PainDetect 11-point NRS.³⁷ The quality and intensity of specific neuropathic symptoms, specifically, burning, prickling, allodynia, attacks, thermal sensitivity, numbness and pressure were gauged from the sensory descriptors of the PainDetect Questionnaire. For each symptom, patients

rated the perceived severity on a 6-point scale (0 = ‘never’; 1 = ‘hardly noticed’; 2 = ‘slightly’; 3 = ‘moderately’; 4 = ‘strongly’; 5 = ‘very strongly’).

The 10-item Pain Self-Efficacy Questionnaire (PSEQ) was used to assess the confidence TN and PPTTN patients (currently) had in performing activities across different areas (e.g., work, leisure, household chores) while experiencing pain.³⁸ Each item response is scored on a 7-point ordinal scale ranging from 0 (not at all confident) to 6 (completely confident). Total scores are determined by the sum of all item responses and range from 0 to 60. Lower scores reflect a patient’s strong focus on their pain whereas higher scores suggest strong self-efficacy beliefs. The PSEQ has good test–retest reliability and internal consistency³⁹ and has been used in previous research with TNI patients.³

Across standardised measures, scores for missing items were imputed from the mean of the other scale items in cases where 10% or less of items were missing (above 10% and the entire scale was considered missing). The only exception to this was for the SFMPQ-2, where if there was one missing item within a subscale, SF-MPQ-2 subscale scores were computed as the average of answered items, and a total score was only calculated in cases where not more than one item was missing on any subscale.

Statistical Analysis

Comparisons between PPTTN and TN patient subgroups on sociodemographic and clinical characteristics, and pain-related, psychosocial and HRQoL indicators were measured using *t*-test, analysis of covariance (ANCOVA) and χ^2 . In instances when continuous data distributions were clearly non-normal, bootstrapping (bias-corrected and accelerated; based on 2000 bootstrap samples) was employed to calculate 95% confidence intervals of mean difference and associated *P* values. Where group comparisons of categorical variables controlled for another variable, binary logistic regression was employed. To evaluate the association between HRQoL indicators

and relevant variables, such as measures relating to pain, mood and sociodemographic and clinical characteristics, Pearson correlation coefficients and Spearman's Rho were calculated according to the distributional properties of the data. The criterion for statistical significance was set at $P < .05$, with no adjustments for multiple comparisons given the descriptive nature of the study. All statistical analyses were completed with the Statistical Package for the Social Sciences, Release 24.0 (SPSS, IBM).

Results

One hundred and thirty-seven (69.9%) patients completed one or more questionnaires and were included in analyses; 97/137 (69.3%) PPTTN patients and 40/56 (71.4%; $P = .768$) TN patients. There was a trend suggesting questionnaires were more likely to be completed by older patients (completers, mean [M] = 52.92, SD = 14.57, non-completers, M = 48.54, SD = 14.61; $P = .056$). But questionnaire completion was not related to gender or clinical features of condition such as duration, trigeminal nerve division affected, number of divisions affected, side of face affected, or presence of headaches/migraines (for all comparisons between completers and non-completers, $P > .14$).

The sociodemographic and clinical characteristics of PPTTN and TN patients completing measures are provided in Table 1. The majority (70% overall) were female. The TN patients were, on average, more than 10 years older than patients with PPTTN. Chronicity of condition (time since onset > 6 months) was high in both patient groups, but duration was significantly longer for TN patients. PPTTN was most common in the mandibular division, while TN affected both the maxillary and mandibular divisions with comparable frequency. PPTTN was predominantly localized in one division or another. In contrast, almost half of the TN patients

had more than one division affected. Symptoms were lateralized approximately equally in both patient groups although a small number of PPTTN patients were affected bilaterally. Almost a quarter of TN patients also suffered from headaches or migraines; this was marginally significantly higher than the rate in patients with PPTTN. TN patients were also more likely than PPTTN patients to have one or more comorbid medical conditions.

TN without persistent pain was diagnosed in 21 (52.5%) of the 40 patients; TN with persistent pain was diagnosed in 19 (47.5%) patients. No precipitant factor was reported in 80% (32) of TN cases. In the remaining cases, a range of (dental) events were recalled by the patients as an initiator(e.g., dental extraction, endodontic treatment, car accident); however, the symptoms, examination and course of the disorder pointed clearly to TN, rather than PPTTN or any other orofacial condition. The aetiology of PPTTN varied widely. PPTTN was sustained during third molar surgery for just under 30% of patients' (TMS; 29 or 29.9%), while in 4 patients, PPTTN was precipitated by extraction of another tooth. PPTTN emerged after repeated extractions or interventions in 16 (16.5%) patients, following implant in 11 (11.3%) patients, and as a result of local anaesthesia in 8 (8.2%) patients. A variety of other causes were identified in 16 (28.6%) patients, including endodontic treatment (2), accidental injury (3), ear/nasal surgery (2) infection (1), and osteotomy (1).The cause was unknown or not recorded in 13 (13.4%) patients.

[Insert Table 1 about here]

Data from clinical assessment (qualitative testing) of sensory symptoms in PPTTN was available for 88 patients. Twenty-three (26.1%) presented with hypoesthesia alone; hypoesthesia was accompanied by paraesthesia in 2 patients, dysesthesia in one patient, allodynia in 2 patients

and a combination of one or more of these symptoms in 6 patients. Paraesthesia alone was observed in 24 patients (27.3%), dysesthesia alone in 4 (4.5%) patients, hyperalgesia alone in 3 patients and allodynia alone in 11 (12.5%) patients. Paraesthesia and dysesthesia was observed in 2 patients, paraesthesia and allodynia in 2 patients, dysesthesia and hyperalgesia in one patient, dysesthesia and allodynia in 2 patients and hyperalgesia and allodynia in 2 patients. Two patients had paraesthesia, hyperalgesia and allodynia while another had paraesthesia, dysesthesia and allodynia.

Affective and Health Function

HRQoL and mood data for the PPTTN and TN samples are shown in Table 2. TN patients tended to score higher on the PHQ-9 than PPTTN patients but differences were not significant. More than half (15 or 53.6%) of patients with TN showed some signs of depression ($\text{PHQ-9} \geq 5$), compared with approximately a third of PPTTN patients (33 or 35.9%; $P = .094$), while moderately severe/severe depression ($\text{PHQ-9} \geq 15$) was evident in a fifth of TN patients (5 or 17.9%) and a tenth of PPTTN patients (10 or 10.9%; $P = .328$). Anxiety levels were highly comparable between participant groups; GAD-7 scores indicated that almost 40% (15 or 38.5%) of TN patients and over a third (33 or 34.4%; $P = .653$) of PPTTN patients experienced clinically significant levels of anxiety ($\text{GAD-7} \geq 8$).

[Insert Table 2 about here]

PPTTN and TN had a marked but comparable effect on patients' OHRQoL. Mean severity scores on the OHIP-14 were higher than the 90th percentile value for the UK dentate population, which ranges from 10-17 across age groups and gender,⁴⁰ and significantly greater

than those observed in a study of patients assessed one week after (successfully) undergoing third molar surgery⁴¹ ($M = 8.6$, $SD = 7.2$, $P < .001$).

While both groups' mean EQ-5D-5L health state valuation scores were less than (EQ-5D-3L) norms observed in age-matched healthy UK populations (which across ten-year age cohorts from 25-75 years range from 0.93 to 0.78),⁴² overall health was significantly poorer in patients with TN than PPTTN. The difference was only marginally significant after accounting for age and presence of comorbid medical condition ($P = .086$), however, suggesting worse HRQoL in TN patients was partly attributable to their older age and greater likelihood of comorbid illness. Nevertheless, post-hoc group comparisons focussed on patients' EQ-5D-5L profile (Fig 1) showed, after controlling for age and comorbid medical condition, significantly worse mobility ($P = .032$) and self-care ($P = .027$) in TN patients compared with PPTTN patients. Pain/discomfort and mood disturbances were domains most affected for both groups, however.

[Insert Fig 1 about here]

Severity of Pain and Sensory Symptoms

The majority of PPTTN (64 or 66.0%) and TN patients (32 or 80.0%; $P = .103$) indicated that they were affected by pain at the time of their consultation and (consequently) completed pain-specific measures (Table 3). Unsurprisingly, overall, these patients reported worse quality of life as evidenced by elevated OHIP-14 scores ($M = 31.81$, $SD = 14.57$ versus $M = 19.64$, $SD = 12.52$, $P < .001$) and lower EQ-Health values ($M = 0.5806$, $SD = 0.2629$ versus $M = 0.8537$, $SD = 0.2081$, $P < .001$).

For those patients completing pain-specific measures, pain severity varied widely across patients. There was a marked difference between diagnostic groups in 4-week strongest pain intensity, however, with TN patients reporting pain at almost ceiling levels. Notably, almost three-quarters of TN patients reported pain that was, on average, severe (i.e., $\geq 7^{43}$; 19 or 73.1%) compared with a little more than half (33 or 55.9%; $P = .135$) of patients with PPTTN. Overall, severity of pain as measured by the SFMPQ-2 was numerically (but not significantly) greater in TN than PPTTN patients. However, examination of the subscales revealed a marked (highly significant) elevation in TN patients' intermittent and affective pain in contrast with continuous and neuropathic pain domains, which were approximately equivalent between TN and PPTTN groups (Fig 2). Self-efficacy for coping with pain was moderate in patients with no difference according to orofacial condition.

[Insert Table 3 about here]

[Insert Fig 2 about here]

The frequency of neuropathic sensory disturbances that were regarded as clinically relevant (i.e., 'strongly' or 'very strongly') for PPTTN and TN participants, gauged from the PainDetect Questionnaire, is shown in Fig 3. More than half of patients with PPTTN reported clinically relevant numbness, a proportion that was significantly greater than that reported by TN patients. In contrast, (electric shock) attacks were a defining feature of TN patients' pain, with just under three-quarters of patients indicating clinically relevant levels compared with approximately 30% of PPTTN patients. Clinically relevant cold/hot pain was also more frequent in TN patients but differences with PPTTN patients were not significant ($P = .183$).

[Insert Fig 3 about here]

Relationships between Pain Characteristics, Affective Function and HRQoL in PPTTN and TN groups

Table 4 shows correlations between generic and oral health-specific QoL indicators and SFMPQ-2 subscales and mood and pain self-efficacy measures for each patient group. In the PPTTN group, across all pain measures, save neuropathic pain for EQ-Health, there were significant moderate associations with HRQoL. Both anxiety and self-efficacy were also moderately related to HRQoL, while PHQ-9 scores were significantly correlated with HRQoL but the magnitude of the association was smaller. In contrast, no pain measure was significantly correlated with TN patients' oral health, although neuropathic pain was marginally significant ($P = .065$), and only intermittent pain showed a strong relationship with TN patients' EQ-Health scores. However, both self-efficacy and anxiety were linked with TN patients' HRQoL. Notably, for both groups age, gender, duration of condition and presence of headaches/migraines, or comorbid medical condition were not significantly related to either HRQoL score (for all associations, $P > .10$). Patients with bodily chronic pain (PPTTN $M = 0.5409$ $SD = 0.2982$; TN $M = 0.4441$, $SD = 0.3522$) showed worse EQ-Health scores than those without (PPTTN $M = 0.7210$ $SD = 0.2504$; TN $M = 0.6250$, $SD = 0.2657$), although the difference was only significant in the PPTTN group ($P = .021$) and not the TN group, where small numbers likely precluded a significant effect ($P = .145$). TN patients with persistent pain had significantly poorer EQ-Health Scores ($M = 0.4692$, $SD = 0.2751$) than did TN patients without persistent pain ($M = .6827$, $SD = 0.2839$; $P = .028$) but there was no difference in OHIP-14 totals ($P = .279$).

[Insert Table 4 about here]

Discussion

To our knowledge, this is the first study directly comparing both the neuropathic symptomatology and psychosocial impact of trigeminal neuralgia to that of (painful) posttraumatic trigeminal neuropathy, using a comprehensive quantitative psychosocial assessment. While OHRQoL and psychological function were comparable between groups, the results showed more severe intermittent and affective pain in TN patients and poorer general health which was partly attributable to their older age and higher prevalence of comorbid medical conditions. All aspects of pain were significantly associated with HRQoL in PPTTN patients only, while anxiety and pain-self efficacy was related to oral and general health in both groups.

Demographics and Clinical Characteristics

Women were over-represented in both PPTTN and TN samples, concurring with several clinical studies and a recent review of population-based studies (TN) that showed greater prevalence in women for both conditions.^{11, 18, 19, 44-46} The reason for the elevated risk of TTN and TN in women remains unclear, although it may be related to gender, the differential manner in which the brains of women respond to the affective dimensions of pain,⁴⁷ which was elevated in TN patients in this study. Also, women are more likely to seek medical care in general and, more specifically, seek advice regarding pain.⁴⁸ TN patients were significantly older than patients with PPTTN, consistent with the findings of previous comparative studies^{18, 23} and those across individual studies of these conditions.^{11, 19, 45, 46} While the incidence of TN is known to increase with age, peaking between 50 and 60 years,^{11, 44} the onset age for PPTTN varies more widely according to the cause of injury.¹⁹

The etiology of PPTTN in the present study varied widely with the greatest percentage attributed to third molar surgery (TMS; 30%). However, this represents a lower value than the percentage of TMS- related PPTTN in previous studies.^{3, 19, 48} When trigeminal nerve injuries do occur as a complication of dental/oral surgical procedures, they usually affect the lingual and/or inferior alveolar branches of the mandibular division and affect the left or right sides at equal rates.⁴⁶ In line with this, PPTTN was most common in the mandibular division of the trigeminal nerve, with approximately equal lateralization, although a small percentage had symptoms on both sides. In contrast, consistent with the somatology relationship of sensory fibres in the trigeminal nerve and previous investigations of TN populations, TN affected both the maxillary and mandibular divisions with a predominance of right-sided symptoms.^{11, 45, 46} Bilateral symptoms were not observed in any TN patients in the present study; bilateral TN appears to be rare except for cases where TN is caused by multiple sclerosis.^{18, 49}

We observed in our TN sample that almost half had TN with concomitant pain, a similar proportion to the Maarbjerg et al.⁴⁵ cohort (49%) but considerably more than in the recent Zakrzewska et al.¹¹ study. It is possible the high rate of TN with concomitant persistent pain in our cohort relates to the referral process, as the clinic has specialist headache neurology input to the assessment and management of patients. Almost a quarter of TN patients also suffered from headaches or migraines; this was significantly higher than in patients with PPTTN, where it was uncommon. Headaches disorders are frequently observed in TN; one recent study identified headache in a quarter of patients and migraines or migraines with tension-type headache in one-fifth.¹¹ Interestingly, Lin and colleagues recently proposed migraine as a previously unidentified risk factor for TN, suggesting the presence of a linked underlying mechanism.⁵⁰ Comorbid medical conditions were also more frequent in TN patients, a likely consequence of their older

age and the association of TN with various systemic diseases such as multiple sclerosis, hypertension and cardiovascular disease.^{51, 52}

Pain Severity and Sensory Symptoms

Most TN and PPTTN patients experienced substantial pain. A minority of patients did not report (problematic) pain at the time of consultation, consistent with previous studies indicating that, at least for some patients presenting in specialist care clinics, TNI may be clinically reflected in a loss of function (anesthesia, hypoesthesia) without pain,^{3, 19} and that frequently in TN, there are changes in sensory quality over the course of the disease.^{11, 53}

There was a tendency for TN patients to report higher levels of pain than patients with PPTTN, most obviously when considering “strongest pain”, which was at ceiling levels. A previous study comparing these patient groups also observed higher ‘typical’ pain levels in TN.¹⁸ TN is considered one of the most painful pain experiences that a patient can report and still no universal treatment is available which can definitely and completely relieve this excruciating, unpredictable pain.⁵⁴ However, examination of patients’ pain experience using the SFMPQ-2 revealed significantly elevated scores for TN patients (relative to PPTTN patients) on intermittent and affective pain subscales only. Intermittent pain attacks are a cardinal sign of TN^{4, 15} and less common after TNI,¹⁹ so the observed difference is not surprising. But the data also indicate that patients with TN may have greater pain-related affective distress than patients with PPTTN. Zakrzewska and colleagues¹¹ observed that more than half of TN patients attending their clinic choose a word from “fearful,” “frightful,” or “terrifying” to describe their pain, attributing high pain catastrophising in this group to unpredictability of the pain attacks.

Interestingly, continuous pain scores were comparable between patient groups, reflecting inclusion in the study of a significant number of TN patients with concomitant persistent pain.

Clinically significant levels of neuropathic symptoms in TN and PPTTN patients were highly similar for burning, prickling, allodynia and pressure (ranging from a quarter to a half of patients across symptoms), reflecting the overlap in symptomatology of the two conditions. More than 50% of patients with PPTTN reported clinically relevant numbness, however, in contrast to just 11% of TN patients. This is consistent with the nature of TNIs, where patients predominantly suffer from neurosensory loss of function in the area supplied by the severed nerve in the form of hypoesthesia or anesthesia.^{46, 55, 56} In contrast, “electric shock” attacks were the defining prominent feature of TN patients’ neuropathic symptomatology, affecting almost three-quarters of patients, consistent with the known characteristics of TN.^{6, 18, 23}

Affective and Health Function

In both TN and PPTTN, patients face limitations in their daily life activities in addition to the overwhelming chronic pain experience. This often leads to psychosocial distress and reduced quality of life.^{11, 48, 57} Our results provide further evidence of the close association between chronic neuropathic orofacial pain, mood disturbance and poor oral and general health.

The burden of orofacial pain condition on overall health was significantly more pronounced in patients with TN compared with PPTTN. Our scores are consistent with those indicating poor quality of life in previous (separate) studies of populations with PPTTN and TN using EQ-5D.^{3, 10} There are two likely explanations for the observed differences. First, the TN patients were older, and as a group more likely to have a comorbid medical illness and (numerically) experience bodily chronic pain, both of which can impair health, especially

Mobility and Self-care domains for which between-group differences were most marked. Second, differences may be attributable to higher intermittent pain levels in the TN group. Intermittent pain was moderately associated with poor HRQoL in both groups, and the only pain dimension linked with HRQoL in the TN group. In a qualitative study, Allsop et al.¹⁵ found TN patients' quality of life was specifically related to fear of pain recurring suddenly and lack of psychological support, in addition to other management-related factors such as delay in diagnosis and side effects of medications. Zakrzewska and colleagues¹¹ have also emphasised the debilitating effects of fear associated with unpredictability of intermittent pain in TN and lack of confidence in dealing with these attacks, and how it results in high pain catastrophizing levels.

Despite more severe (intermittent and affective) pain in TN patients, PPTTN and TN patient groups evidenced comparably impaired OHRQoL. It is well established that altered sensation in the orofacial region as a result of TNI can interfere with a number of functions including eating, drinking, kissing, make up application, shaving, and tooth brushing, all of which affect patients' quality of life.^{19, 46} One recent study found that enjoying social contact with other people, the ability to eat and enjoy food and maintaining an emotional state without irritability were the most affected aspects of health function affected in a group of TNI patients.⁵⁸ Similar functional problems are also experienced by TN patients.^{6, 59} But interestingly, whereas - in line with previous studies of patients with PPTTN - neuropathic pain severity showed a moderate-to-strong relationship with oral health,³ no aspect of pain was reliably linked with OHRQoL in TN patients, suggesting that the extent of functional impairment for activities that involve the face are not necessarily related to the frequency or intensity of TN pain attacks.

The disability experienced by PPTTN and TN patients is consistent with the high levels of anxiety and depression evidenced by both groups. Observed levels of anxiety and depression

were in line with those shown in other (separate) studies of patients with PPTTN and TN,^{3, 11, 60} indicating mood disturbances, particularly anxiety disorders, are prevalent in these conditions. TN patients may be at greater risk of depression than patients with PPTTN, broadly consistent with the elevated levels of affective pain distress we observed in this group as well as studies showing a close relationship between pain severity and depression in patients with neuropathic orofacial pain.^{3, 12}

The findings of affective and psychological dysfunction in both patient groups, which was severe in 15-20% of cases, supports calls for the routine use of holistic, multidisciplinary approaches for pain management in PPTTN and TN patients.^{11, 61} Significantly, anxiety and pain self-efficacy were reliably associated with oral and general health in both groups. In TN patients, psychological function was more closely related to oral health status than any measure of pain and only intermittent pain better correlated with general health, indicating that mental health status of these patients is closely linked with pain-related disability. Galli and colleagues⁶² found that (after controlling for pain severity) beliefs about illness, particularly that pain could have serious consequences on one's life and low personal control, negatively impacted on treatment outcomes in a group of patients with orofacial pain that included individuals with TN. In patients with temporomandibular muscle and joint disorders, both worry about pain and depression have been shown to contribute to the progression of chronic pain disability.²¹ More generally, neural markers for fear and anxiety which exacerbate chronic pain have been identified.⁶³ As such, psychological-based interventions (e.g., cognitive behavioural therapy) that target psychosocial components in patients with TN and PPTTN, such as pain-related anxiety, illness beliefs, and affective dimensions of orofacial pain, may usefully complement aspects of treatment concerning medication management and rehabilitation.^{11, 61}

Study Limitations

The study was cross-sectional and, as such, pain severity and psychosocial constructs were assessed at a single time point only not allowing specification of the nature of identified relationships between pain, psychosocial factors and quality of life. Further, the psychological and health status of patients prior to nerve injury or onset of TN is unclear. A recent retrospective study of patients with orofacial neuropathic pain found a history of chronic stress and psychological/psychiatric illness in 37% of cases,⁶⁴ suggesting a high rate of psychological dysfunction prior to onset of orofacial pain. Additionally, the study involved a population of patients who attended a specialist national clinic and may not be representative of the wider population of patients with TNI and TN (who may not be as severely affected). Also, not all patients attending the clinic completed measures. However, this was not related to orofacial condition or clinical profile suggesting the samples were representative of referred patients. The sample size of TN patients was relatively small (compared with the PPTTN sample) and heterogeneous, which may have contributed to the inability to detect statistically significant effects on some outcomes, precluded multivariate analysis of factors associated with oral and general HRQoL (identified from bivariate analyses), and did not readily allow comparisons of important subgroups. Additionally, as previously noted, TN patients were older and more often had a comorbid medical illness than patients with PPTTN, complicating comparisons of affective and health function. Finally, there was no correction for multiple group comparisons, raising the risk of Type I errors.

Conclusions

Both TN and PPTTN are associated with a significant psychosocial burden and reduced quality of life. While oral health is affected equally in TN and PPTTN, reflecting the loss of function for activities that involve the face associated with both conditions, TN has a more marked impact on overall health in comparison to PPTTN. Neuropathic pain intensity is higher in TN than PPTTN, notably for aspects closely related to pain attacks that characterise the former, such as strongest pain endured and intermittent and affective pain dimensions. TN patients also appear to be at greater risk of depression, although clinically significant anxiety is comparably high in both groups, evident in up to 40% of patients. The substantial burden of illness observed here, in addition to the close associations between anxiety and pain self-efficacy and oral and general HRQoL in both groups, suggest a need for psychological support to be integrated into the management programmes of both conditions to help patients cope better with their chronic disorder and improve efficacy of treatment.

Statement of Conflict of Interest

The authors state no conflict of interest.

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Figure legends

Fig 1 EQ-5D-5L profile (percentage reporting problems in each dimension) of painful post-traumatic trigeminal neuropathy (PPTTN) and trigeminal neuralgia (TN) patients. Note: Data labels represent percentages; for Mobility, Self-care, Usual activities and Anxiety/Depression dimensions, TN $n = 39$; * Indicates significant differences between groups after controlling for age ($P < .05$).

Fig 2 Mean scores on Short Form McGill Pain Questionnaire – 2 (SFMPQ-2) subscales (0-10). Note: PPTTN = painful post-traumatic trigeminal neuropathy; TN = Trigeminal neuralgia; Data labels represent mean values; Error bars represent the standard error of the mean; n values for subscales are variable due to missing responses on some SFMPQ-2 items; * Indicates significant differences between groups ($*P < .05$; $**P < .001$).

Fig 3 Frequency (percentage of patients) indicating clinically relevant problems (i.e., score > 3) on dimensions of neuropathic pain in the PainDetect Questionnaire. Note: PPTTN = painful post-traumatic trigeminal neuropathy; TN = trigeminal neuralgia; Data labels represent percentages; n values for dimensions are variable due to missing responses on some PainDetect Questionnaire items; ** Indicates significant differences between groups ($P < .001$).

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Table 1. Demographic and Clinical Characteristics of Patients with Painful Post-Traumatic Neuropathy (PPTTN) and Trigeminal Neuralgia (TN). Numbers represent frequency (percentage) unless otherwise stated.

Variable	PPTTN (n = 97)	TN (n = 40)	PPTTN vs. TN (<i>P</i> value)
Sociodemographic			
Gender: Female	70 (72.2%)	26 (65.0%)	.405
Age (Mean [SD])	49.4 (13.8)	61.3 (13.1)	<.001
Clinical Characteristic			
Duration (Mths;Median[IQR])	13.0 (5.0-36.0)	34.0 (12.0-78.0)	.039
>6 months	61 (67.8)	31 (93.9)	.002
<u>Division affected</u>			
Ophthalmic (V1)	0 (0.0)	2 (5.0)	
Maxillary (V2)	23 (24.2)	9 (22.5)	
Mandibular (V3)	64 (67.4)	11 (27.5)	
Ophthalmic and Maxillary (V1, V2)	1 (1.1)	4 (10.0)	
Maxillary and Mandibular (V2, V3)	3 (3.2)	12 (30.0)	
Ophthalmic, Maxillary and Mandibular (V1,V2,V3)	3 (3.2)	2 (5.0)	<.001
More than one division affected	8 (8.4)	18 (45.0)	<.001
<u>Side affected</u>			
Left	45 (46.9)	17 (42.5)	
Right	41 (42.7)	23 (57.5)	
Both	10 (10.4)	0 (0.0)	.061
Headaches or Migraines	11 (11.3)	9 (23.1)	.080
Other (Bodily) Chronic Pain	13 (13.4)	10 (25.0)	.099
Comorbid Medical Condition(s)	25 (25.8)	18 (45.0)	.027

Note: IQR = inter-quartile range; Co-medical conditions included (but were not limited to) hypertension, diabetes, hypothyroidism, multiple sclerosis, epilepsy, hiatus hernia, cardiovascular disease, and/or malignancy; there was a small number of missing data on some variables stated percentages and means refer to participants with data available for variable in question; significant differences between groups are highlighted in bold.

Table 2. Affective Function and Health-Related Quality of Life (HRQoL) in Painful Post-Traumatic Neuropathy (PPTTN) and Trigeminal Neuralgia (TN) Patients.

Questionnaire	PPTTN		TN		PPTTN vs TN	
	n	Mean (SD)	n	Mean (SD)	Mean difference (95% CI)	<i>P</i>
<u>Mood</u>						
PHQ-9 (0-27)	92	4.74 (6.54)	28	6.89 (6.76)	-2.15 (-5.17,0.64)	.145
GAD-7 (0-21)	96	6.09 (5.95)	39	5.97 (5.65)	0.12 (-2.08,2.32)	.915
<u>HRQoL measures</u>						
OHIP Severity (0-56)	97	28.57 (15.02)	38	27.61 (15.21)	0.96 (-4.82,6.56)	.739
OHIP Extent (0-14)	97	5.92 (4.33)	38	5.87 (4.36)	0.49 (-1.49,1.59)	.863
EQ Health (-0.285 - 1.00)	97	0.6969 (0.2630)	39	0.5786 (0.2964)	0.1182 (0.0111,0.2192)	.031
EQ VAS (0-100)	97	69.78 (22.94)	39	64.00 (23.41)	5.78 (-2.53,14.48)	.211

Note: n values for questionnaires are variable due to a small number of patients not completing all measures; *P* values were calculated using independent group *t*-tests; PHQ-9 = Patient Health Questionnaire – 9; GAD-7 = Generalized Anxiety Disorder - 7; OHIP = Oral Health Impact Profile; EQ Health = EQ-5D-5L health state evaluation; EQ VAS = current overall health rating; significant differences between groups are highlighted in bold.

Table 3. Pain and Pain-Self Efficacy in Painful Post-Traumatic Neuropathy (PPTTN) and Trigeminal Neuralgia (TN) Patients.

Questionnaire	PPTTN		TN		PPTTN vs TN	
	n	Mean (SD)	n	Mean (SD)	Mean difference (95% CI)	<i>P</i>
<u>Pain (PDQ; 0-10)</u>						
Pain now	59	5.19 (2.71)	26	4.31 (3.16)	0.88 (-0.46,2.31)	0.222
Strongest pain	59	7.22 (2.67)	26	8.50 (1.86)	-1.28 (-2.23,-0.25)	0.016
Average pain	59	6.03 (2.73)	26	7.04 (2.34)	-1.01 (-2.23,0.22)	0.107
SFMPQ-2 (Total; 0-10)	59	3.18 (2.25)	19	3.89 (2.05)	-0.71 (-1.87,0.45)	0.228
PSEQ (0-60)	60	34.55 (15.28)	27	35.56 (15.76)	-1.01 (-8.12,6.10)	0.779

Note: n values for questionnaires are variable due to a small number of patients not completing all measures; *P* values were calculated using independent group *t*-tests; PDQ = PainDetect Questionnaire, SFMPQ-2 = Short Form McGill Pain Questionnaire – 2; PSEQ = Pain Self-Efficacy Questionnaire; significant differences between groups are highlighted in bold.

Table 4. Associations Between HRQoL, Pain Characteristics and Affective Function in Painful Post-Traumatic Neuropathy (PPTTN; n = 97) and Trigeminal Neuralgia (TN; n = 40) Groups.

Questionnaire	PPTTN		TN	
	OHIP Severity	EQ Health	OHIP Severity	EQ Health
SFMPQ-2				
Continuous	0.48**	-0.49**	0.03	0.05
Intermittent	0.52**	-0.47**	0.34	-0.61*
Neuropathic	0.67**	-0.20	0.39	0.03
Affective	0.44**	-0.43**	0.24	-0.09
PHQ-9	0.30**	-0.39**	0.22	-0.18
GAD-7	0.42**	-0.57**	0.45*	-0.33*
PSEQ (0-60)	-0.45**	0.56**	-0.61**	0.44*

Note: Values presented are Pearson *r* or Spearman rho (according to distribution of correlated variables); n values for SFMPQ-2 subscales are maximum of 61 for PPTTN and 23 for TN; OHIP = Oral Health Impact Profile; EQ Health = EQ-5D-5L health state evaluation; SFMPQ-2 = Short Form McGill Pain Questionnaire – 2; PHQ-9 = Patient Health Questionnaire – 9; GAD-7 = Generalized Anxiety Disorder - 7; PSEQ = Pain Self-Efficacy Questionnaire. **P* < .05, ***P* < .001.

Fig 1

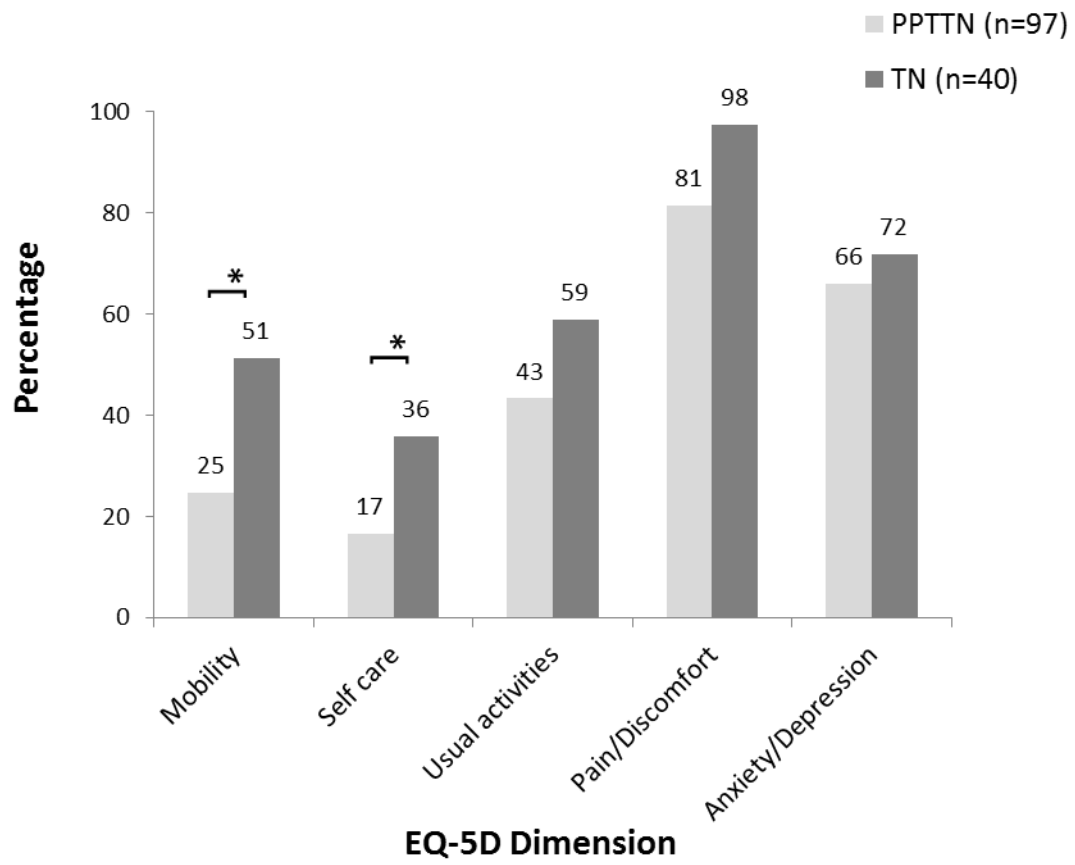


Fig 2

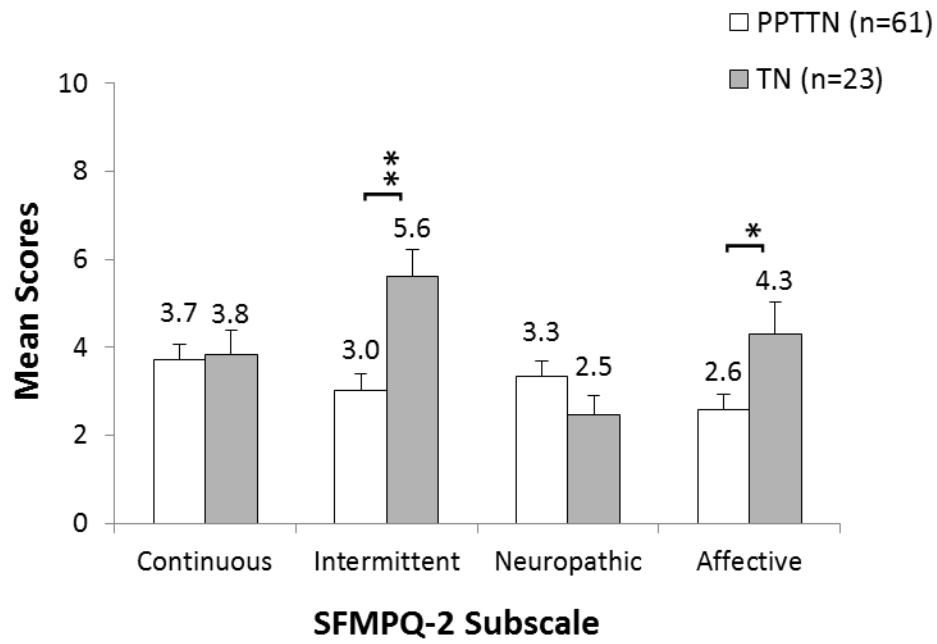


Fig 3

